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How Good Is Your Rule of Thumb? Validating Male-to-Female Case Ratio as a Proxy for Men Who Have Sex With Men Involvement in *N. gonorrhoeae* Incidence at the County Level

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Abstract

Background: Lacking information on men who have sex with men (MSM) for most reported cases, sexually transmitted disease (STD) programs in the United States have used crude measures such as male-to-female case ratios (MFCR) as a rule of thumb to gauge MSM involvement at the local level, primarily with respect to syphilis cases in the past. Suitability of this measure for gonorrhea incidence has not previously been investigated.

Methods: A random sample of gonorrhea cases reported from January 2010 through June 2013 were interviewed in selected counties participating in the STD Surveillance Network to obtain gender of sex partners and history of transactional sex. Weighted estimates of proportion of cases among MSM and proportion reporting transactional sex were developed; correlation between MFCR and proportion MSM was assessed.

Results: Male-to-female case ratio ranged from 0.66 to 8.7, and the proportion of cases occurring among MSM varied from 2.5% to 62.3%. The MFCR was strongly correlated with proportion of cases among MSM after controlling for transactional sex (Pearson partial r = 0.754, P < 0.0001).

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Conclusions: Male-to-female case ratio for gonorrhea at the county level is a reliable proxy measure indicating MSM involvement in gonorrhea case incidence and should be used by STD programs to tailor their programmatic mix to include MSM-specific interventions.

Recent analysis of trends in reported cases of gonorrhea show that case rates are increasing nationally with a 23.6% increase in the overall rate of reported cases between 2010 and 2015 from 100.2 to 123.9 cases per 100,000.[1] Increases in reported cases among men contribute significantly to observed changes in gonorrhea case rates; the rate among men increased 50.1% during this timeframe compared with a 1.5% increase among women. Evidence also suggests that cases among men who have sex with men (MSM) may be common and increasing in many locations.[2–5]Changes in the proportion of cases occurring among MSM at the local level may have important implications for gonorrhea control efforts because of differences in screening recommendations and optimal disease control strategies between MSM and exclusively heterosexual men and women. It seems reasonable to consider that uncomplicated gonococcal infections among men who have exclusively male sex partners may be less likely to have reproductive health consequences than infections in heterosexual women and men. A public health response for gonorrhea among MSM focused primarily on frequent screening among those reporting exclusively male partners, and promptly treating all identified infections may be an appropriate infection control strategy for this population.

The male-to-female case ratio (MFCR), which compares the number of reported male cases to reported female cases, has been used by sexually transmitted disease (STD) programs as a rule of thumb to inform syphilis epidemiology and control measures.[6] Higher male-to-female case and case rate ratios are characteristics of either sex worker involvement in syphilis clusters or, as has recently been observed in the United States and globally, broadly resurgent syphilis among MSM.[7–9] Many STD control programs prioritize syphilis control and conduct public health case finding and partner management with early syphilis cases, including documenting the gender of sex partners, which is increasingly well characterized for a large proportion of syphilis cases.[10] The potential for fetal loss and infant mortality associated with congenital syphilis makes ascertaining the gender of sex partners, interrupting the chain of transmission and assuring treatment a continuing public health priority.[11]

Conversely, very few STD programs have complete gender of sex partner information for patients reported with gonorrhea. The majority of reported cases are identified through laboratory reporting and not routinely prioritized for partner services because of the increasing volume of cases and decreasing public health resources for case follow-up. Sentinel surveillance projects indicate that a significant proportion of male gonorrhea cases occur among MSM.[1] Many gonococcal infections are asymptomatic; transmission can occur at any time during infection, and identification of cases is often dependent on routine screening.[12,13] The general principal that the MFCR for reported gonorrhea cases can be an indicator of MSM involvement in local incidence, as it is for syphilis, is often presumed. In the absence of comprehensive, case-level information on the gender of sex partners reported by providers or obtained from partner management interviews for a large proportion of gonorrhea cases, this easily calculated ratio may be a programmatically useful indicator of the extent of MSM involvement in local gonorrhea case incidence. The objective of this

analysis was to examine the correlation between the MFCR and proportion of overall gonorrhea cases attributable to MSM at the county level among geographically diverse jurisdictions collaborating in an enhanced surveillance project systematically collecting behavioral information on a representative sample of reported gonorrhea cases.

METHODS

Investigators in state or city health departments collaborating in the CDC-funded STD Surveillance Network (SSuN) randomly sampled and investigated gonorrhea cases diagnosed and reported between January 2010 and June 2013 for all counties in their jurisdictions. Following common protocols, patients in the sample were contacted and interviewed by public health staff. Data on sex of sex partners was obtained in the course of a comprehensive behavioral interview. We defined MSM for our analysis as any male patient reporting male sex partners in the exposure period (previous 2–3 months) and/or reporting their sexual orientation as gay or bisexual. We chose to include both self-reported orientation as well as partner data to reflect the most inclusive definition of MSM for developing our estimates. Patients were also asked about transactional sex, defined as exchanging money or drugs for sex, or vice-versa, in the previous 12 months, which is the time interval used for collecting most behavioral characteristics in SSuN.

Analytic weights were developed for interviewed cases accounting for sample fraction at the county level and adjusting for nonresponse by gender and age group of the patient. These case weights were used to estimate the proportion of gonorrhea cases occurring among MSM by county and the proportion of all cases reporting any transactional sex. We also obtained a full census of cases reported in these counties from the National Electronic Telecommunications Surveillance System and calculated the maleto-female case ratio for each county. The SSuN protocols allowed for variation in sample fraction at the county level, reflecting local capacity to implement the project and conduct interviews. For the purposes of this analysis, we selected only counties reporting 100 or more cases and with at least 10% sampled for investigation during the study period to minimize variance due to small case counts (Table 1). We excluded one additional county from our analysis (San Francisco, CA) because more than 90% of all cases were reported among men, the overwhelming majority of whom (84.1%) were MSM. Our objective was to validate MFCR as an indicator for MSM contribution to the gonorrhea burden in mixed epidemic contexts.

We plotted the proportion of cases occurring among MSM versus the male-to-female case ratio by county and calculated Pearson r to assess the strength of correlation. We also examined the proportion of patients reporting transactional sex and calculated Pearson partial r to assess the association between the male-to-female case ratio and proportion of cases reported among MSM after adjusting for this potential confounder. Transactional sex reported by females in our data was exclusively heterosexual and increases the number of males exposed. This would result in additional males being infected, increasing the MFCR. Transactional sex reported by MSM was among male partners and would similarly affect the MFCR. To partially address this possible bias, we calculated Taylor series 95% confidence intervals for MSM and transactional sex estimates and conducted a sensitivity analysis assuming the lower 95% confidence limit for MSM cases and the upper estimate of

transactional sex and repeated our analysis using these limit value estimates. All analyses were conducted using SAS 9.3 (SAS Institute, Cary, NC).

RESULTS

We selected counties reporting 100 or more cases (56/127, 44.1%) to maximize the robustness of our MSM and transactional sex estimates. Counties with fewer than 100 cases were more rural, with crude MFCR values closer to 1 (mean, 1.03 vs 1.27 for the included counties), with a lower proportion of cases estimated to be MSM (mean, 20.1% vs 22.3% for the included counties) and fewer patients reporting transactional sex (mean, 2.5% vs 2.8% for the included counties). Counties that met our inclusion threshold cumulatively reported 238,689 cases of gonorrhea during the study period. Thirty-eight thousand four hundred twenty-six (16.1%) cases were randomly selected for enhanced investigation, and patient interview data were obtained for 16,967 cases for an interview response rate of 44.2%. Male-to-female case ratio in the selected counties ranged from 0.66 to 3.1, and the proportion of total cases attributable to MSM varied at the county level from 0% to 62.3%. Scatterplot (Fig. 1) of the MFCR versus estimated proportion of cases among MSM in the selected counties suggested a roughly linear relationship between these two values at the county level. The Pearson correlation coefficient was significantly different from zero (0.769, $P < 0.0001$), demonstrating that for these 56 counties, MFCR was strongly correlated with the estimated proportion of male cases reporting same-sex partners.

Adjusting for the proportion of patients reporting transactional sex (2.4% overall; range, 0–17%), the resulting Pearson partial r was 0.754 ($P < 0.0001$), indicating that correlation remained strong between MFCR and proportion of cases occurring among MSM, independent of proportion of cases reporting transactional sex. When we repeated this analysis using the lower bound of the 95% confidence limit for proportion of cases reported among MSM and the upper bound estimate for proportion reporting transactional sex, we found that Pearson partial r (0.877, $P < 0.0001$) suggests a slightly stronger correlation between MFCR and proportion of cases reported among MSM.

DISCUSSION

Our findings support the intuitive assumption that there is a strong correlation between the proportion of reported gonorrhea cases occurring among MSM and the male-to-female cases ratio at the county level. Moreover, transactional sex did not significantly modify the strength of the correlation in our analysis, although we found very few patients reporting transactional sex in our sample. Our findings would not rule out the possibility that localized clusters of cases can occur where transactional sex might be the primary driving factor associated with MFCR, and we would suggest that very high or anomalous male-to-female case ratios should be further investigated. The interventions and possible reproductive health sequela would differ for heterosexual outbreaks, such as those associated with sex work, versus those primarily occurring among MSM. It is also possible that differential screening practices for women, or for MSM, may lead to more cases being diagnosed and reported in 1 gender.

Yet our results do provide evidence that high male-to-female case ratios are correlated with MSM involvement in gonorrhea transmission. The male-to-female case ratio is easily calculated from available case reporting data and may provide more timely insight to inform STD control programs. Moreover, our results are generated based on cases reported by county, which may be a geographically useful level supporting intervention mixes responsive to variations between counties within a state. The STD programs can frequently measure changes in the crude male-to-female case ratio based on timely case reporting or laboratory reporting information and should consider ratio values above 1 in a geographic area as an indicator of possible MSM involvement warranting additional investigation or intervention targeting. Periodic reassessment of the relationship between MSM and MFCR should also be undertaken where reliable information on gender of sex partners is available for a representative sample of cases.

There are several important limitations to this analysis. Although there is geographic diversity represented in SSuN jurisdictions, sites were chosen for participation through competitive processes and are not necessarily representative of the entire United States. The interview completion rate across the participating jurisdictions was 44.2%; we examined the distribution of respondents to sampled cases and observed only minor differences in response rates by sex, with women slightly (<2%) more likely to respond than men. The most pronounced difference in response was observed by age group, with 20 to 25-year-old patients more likely to complete interviews (4%) and those 45 years or older less likely to respond (4.9%). Nonresponse weights were calculated to adjust for these minor differences in response in our analysis.

Additionally, estimates of the proportion of reported cases that occur among MSM and the proportion reporting transactional sex are based on self-report from a sample of cases and are subject to potential social desirability biases. Although we adjusted our interview data for nonresponse by gender and by age group in our weighting procedures, unmeasured sources of bias may still exist. However, among randomly selected male patients interviewed for this project, fewer than 2% (165 cases) refused to identify either their sexual orientation or gender of sex partners; we do not believe that there was significant underreporting of MSM status among the patients we interviewed.

Differential screening patterns may also influence disease detection and reporting, especially among women. This may also be the case in the future for MSM as recommendations to screen all exposed nongenital anatomic sites are fully implemented. The proportion of MSM versus women reporting transactional sex may also be influenced by different local patterns, which could have an effect on the male-to-female case ratio. Results of our sensitivity analysis suggest that transactional sex may also be independently correlated with the MFCR. In our data, a fairly small proportion of both heterosexual women and MSM reported transactional sex (at 2.5% and 4.3%, respectively), which in either scenario likely results in local incidence pattern reflective of more male than female exposures per index case which would lead to increases in MFCR.

CONCLUSIONS

Our data suggest that the MFCR for gonorrhea at the county level may be a reliable and useful indicator of MSM involvement and could be used by STD programs to tailor their local programmatic mix to include MSM-specific interventions. Jurisdictions should continue to attempt to ascertain sex of sex partners for all reported cases where resources permit and continue to use those data to help prioritize cases for follow-up. However, where such information is incomplete, MFCR provides a supplemental source of information to help prioritize interventions. Where MSM are found to constitute a large proportion of cases, interventions might include deemphasizing individual partner services in favor of intensified provider-level efforts to assure routine screening at all anatomic sites, along with prompt treatment of all identified infections with recommended regimens. Where resources permit, and data indicate a primarily heterosexual incidence pattern, partner services might be prioritized for women at risk of adverse reproductive health outcomes.

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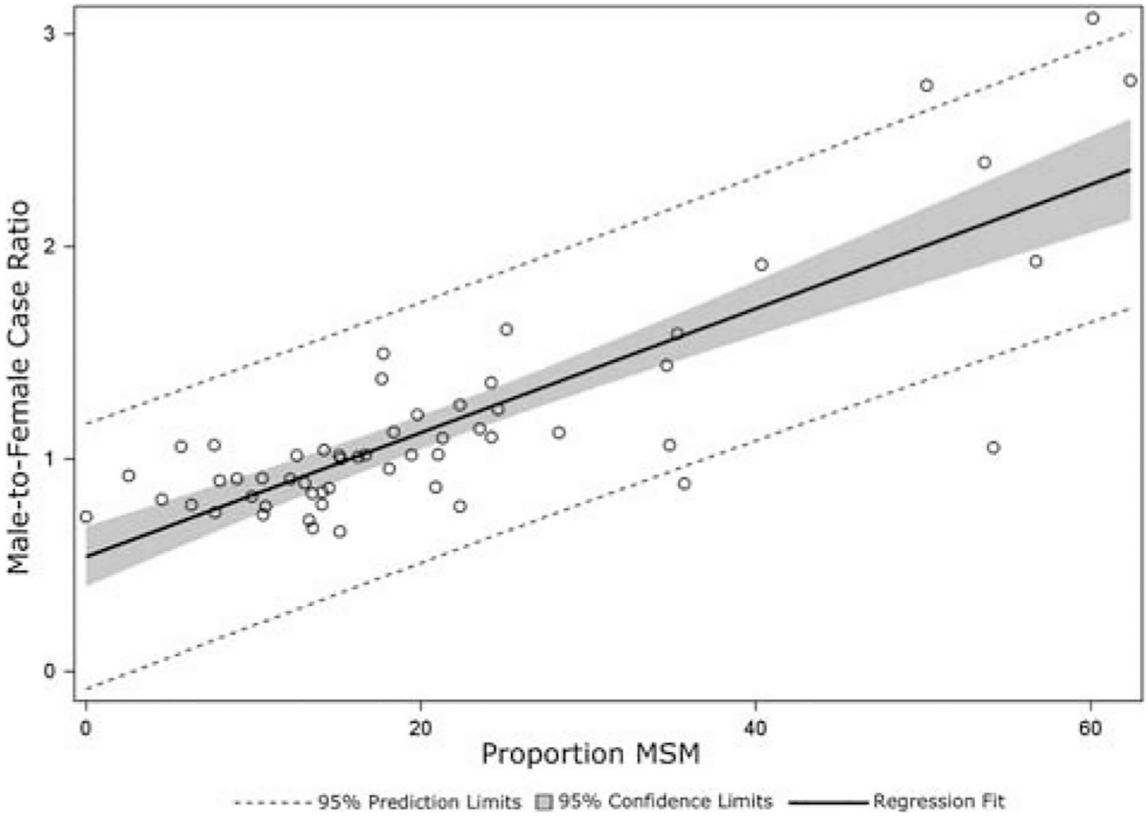

Figure 1.

Scatter plat and linear regression fit of male-to-female gonorrhea case ratio versus proportion of gonorrhea cases reported among MSM, 56 SSuN Counties, 2010–2013.

TABLE 1.

Contributing SSuN Sites, Number of Cases, MFCR and Estimated Proportion of Cases Occurring Among MSM, January 2010 to June 2013

SSuN Site*	No. Cases	MFCR†	%MSM‡
Alabama (1 county)	6580	0.81	4.38
Baltimore city (1 city)	8669	0.89	12.96
California (30 counties)	—	—	—
06001	5714	1.25	22.33
06007	227	0.91	9.01
06013	3045	0.71	13.32
06019	4213	0.75	7.72
06023	215	1.02	16.69
06025	124	1.07	7.65
06029	3889	1.06	5.66
06033	143	0.67	13.54
06037	37,976	1.91	40.34
06047	278	0.95	18.11
06053	564	1.04	14.21
06059	3991	1.93	56.74
06061	295	1.05	54.18
06065	3518	1.13	18.37
06067	6922	0.87	20.89
06071	5197	0.86	14.49
06073	8257	2.39	53.65
06077	2399	0.90	7.97
06079	189	1.36	24.20
06081	845	2.76	50.21
06083	380	1.12	28.25
06085	2770	1.59	35.32
06087	300	1.23	24.60
06089	332	0.92	2.53
06095	1155	0.74	10.58

SSuN Site*	No. Cases	MFCR†	%MSM‡
06097	506	1.61	25.11
06099	791	1.07	34.84
06101	105	0.73	0.00
06111	796	1.10	21.29
06113	234	1.49	17.75
City of Chicago (1 city)	29,547	0.90	11.88
Colorado (1 county)	6046	1.14	23.31
Connecticut (2 counties)	—	—	—
09003	2275	0.78	6.30
09009	2203	0.82	9.89
Louisiana (1 Parish)	4845	0.91	10.43
New York City (5 Counties)	—	—	—
36005	9805	1.02	19.43
36047	11,649	1.21	19.77
36061	16,646	2.78	62.37
36081	6365	1.38	17.66
36085	766	0.79	14.08
Philadelphia city (1 county)	23,659	1.02	12.54
Virginia (2 counties, 1 city)	—	—	—
51,041	764	0.84	13.49
51,087	760	0.84	14.13
51,760	2660	0.78	10.72
Washington (10 counties)	—	—	—
53,005	185	0.66	15.16
53,011	536	1.10	24.23
53,033	5376	3.07	60.13
53,035	193	1.02	21.03
53,053	1947	1.01	16.23
53,061	597	1.44	34.66
53,063	605	0.78	22.33
53,067	238	1.02	15.13

SSuN Site*	No. Cases	MFCR†	%MSM‡
53,073	127	0.88	35.74
53,077	276	1.00	15.21
SSuN Total	238,689	1.21	24.48

*State/City (counties identified by Federal Information Processing Standards Codes).

†Male-to-female case ratio for included jurisdictions.

‡Estimated proportion of all reported cases occurring among MSM.